REMARKS

Claims 4 - 15, 18-23, and 39 – 47, and 49 - 51 are pending. Claims 39 and 40 have been amended to recite that the microstructures comprise a structural matrix and claim 48 has been canceled. Support for these amendments is found throughout the specification, for example at page 13, lines 13-28. Claims 21, 22, 49 and 50 have been amended to recite particular active agents, as supported at page 19, lines 5 - page 20, line 6. Applicants respectfully submit that no new matter is added by these amendments and respectfully requests entry thereof.

Claims 4-15 and 18-23 have been objected to as being of improper dependency for depending on a later-numbered claim. Applicants respectfully submit that this objection is improper. The Examiner is requested to withdraw this objection and renumber the claims upon allowance to reconcile proper claim numbering.

Claims 4-15, 39-47, 49, and 50 have been rejected under 35 U.S.C. 103 as being obvious over Hanes et al. in view of WO 94/04133 or Yen. As set forth by the Examiner, Hanes et al. discloses various features of the present invention, but is silent as to the use of calcium in the composition or the pore sizes of the present invention.

WO 94/04133 (Simpkin et al.) is directed to a dry powder for inhalation comprising at least one microfine drug and a carrier. The carrier of Simpkin et al. is not a matrix in which the drug is dispersed, but rather consists of discrete particles which are typically much larger than the particles comprising the active agent. Such blends of active agent-containing particles and carrier particles without active agent are conventional in the art (See Simpkin et al., page 1, fourth paragraph, page 2, first and second full paragraphs, and the paragraph bridging pages 5-6). Simpkin et al. discloses calcium carbonate as a suitable carrier material. It is essential in the teachings of Simpkin et al. that the carrier particles are a separate and discrete particle population in the composition of Simpkin et al. As mentioned in Simpkin et al. (page 2, first paragraph and well known in the art), the use of such carrier materials is necessary due to the otherwise poor flow properties of the active-containing particles.

Claims 39 and 40 have been amended to recite that the composition of the present invention comprises a structural matrix. None of the prior art of record discloses or

suggests a structural matrix comprising phospholipid and calcium as currently recited in claims 39 and 40. Simpkin et al. teaches away from providing the calcium carbonate carrier together with the active microfine particles as a single structural matrix. Such a modification is clearly contrary to the need in Simpkin et al. of addressing the required performance characteristics of the powders disclosed in Simpkin et al. since the larger carrier particles are required for purposes of dispersibility. Therefore, Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

Yen relates to methods of making protein nanomatrices and products obtained thereby. The nanomatrices of Yen are intended for injection and are not concerned with inhalation. None of the prior art of record discloses or suggests a structural matrix comprising phospholipid and calcium as currently recited in claims 39 and 40. Yen fails to disclose or suggest a structural matrix comprising phospholipid and calcium as currently recited in claims 39 and 40. Thus, Yen does not satisfy the deficiencies of Hanes et al. and Simpkin et al. for the reasons set forth above. Thus, the rejection is improper and should be withdrawn.

Claim 51 has been rejected as being obvious over Hanes et al. in view of WO 94/04133 and further in view of Igarashi et al. Igarashi et al. is relied upon for teaching the use of aminoglycoside antibiotics for the treatment of gram-positive and gram-negative bacteria. The examiner further notes that Igarashi et al. teaches the use of calcium carbonate for the composition.

Applicants respectfully submit that Igarashi et al. fails to satisfy the deficiencies of Hanes et al. and Simpkin et al. for all of the reasons set forth above as it does not suggest providing a structural matrix of phospholipid and calcium as claimed. Thus, Applicants respectfully submit that the rejection has been overcome and should be withdrawn.

Additionally, claim 48 was not included in the rejection of the claims over prior art in the Outstanding Office Action. Applicant has further amended claim 40 to include the recitation of claim 48 that the phospholipid comprises a gel to liquid crystal transition temperature of greater than 40° C.

Applicants believe that all of the pending claims are presently in condition for allowance. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

If it is believed that this will expedite prosecution of the present application, the Examiner is invited to telephone the undersigned attorney at the number below

Respectfully submitted,

Date: 9/19/02

By: _____

Michael Rafa
Reg. No. 38,740
Ph. (650) 631-5053

Version with Markings to Show Changes Made

In the Claims

21. The powder of claim 20 wherein said bioactive agent is selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, antiinfectives, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics, anesthetics, anti-tuberculars, antivirals, immunoactive agents, vaccines, immunosuppressive agents, imaging agents, cardiovascular agents, enzymes, steroids, DNA, RNA, viral vectors, antisense agents, proteins, peptides and combinations thereof.

22. The powder of claim 20 wherein the bioactive agent is selected from the group consisting of [nicotine], fentanyl, morphine, lung surfactant, [PTH], leuprolide, interferon, insulin, budesonide formoterol, goserelin, and growth hormones.

39. A powder composition comprising a plurality of particulate microstructures, said microstructures comprising a structural matrix comprising an active agent, calcium and a phospholipid, wherein said microstructures comprise a geometric diameter of 1-30 microns, an aerodynamic diameter of less than 5 microns, and a bulk density of less than about 0.5 g/cm^3.

40. A powder composition comprising a plurality of particulate microstructures, said microstructures comprising a structural matrix comprising calcium and a phospholipid wherein said phospholipid comprises a gel to liquid crystal transition temperature of greater than 40° C.

Claim 48 has been canceled.

49. The powder of claim 43 wherein said active agent is a bioactive agent selected from the group consisting of antiallergics, bronchodilators, pulmonary lung surfactants, analgesics, antibiotics, antiinfectives, leukotriene inhibitors or antagonists, antihistamines, antiinflammatories, antineoplastics, anticholinergics, anesthetics, anti-

tuberculars, antivirals, immunoactive agents, vaccines, immunosuppressive agents, imaging agents, cardiovascular agents, enzymes, steroids, DNA, RNA, viral vectors, antisense agents, proteins, peptides and combinations thereof.

50. The powder of claim 49 wherein the bioactive agent is selected from the group consisting of [nicotine], fentanyl, morphine, lung surfactant, [parathyroid hormone], leuprolide, interferon, insulin, budesonide formoterol, goserelin, and growth hormones.